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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,181	11/16/2001	Avi J. Ashkenazi	P2730P1C53	3268

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EXAMINER	
KEMMERER, ELIZABETH	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,181	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-128 and 131-138* is/are rejected.

7)☒ Claim(s) *129 and 130* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The preliminary amendments of 16 November 2001 and 03 September 2002 have been entered in full. Claims 1-118 are canceled. Claims 119-138 are under examination.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 24 May 2002 has been considered by the examiner. However, since the Blast results cited therein are not true publications with a publication date, they are not fully in compliance with 37 CFR 1.97 and thus they will not be printed on the face of the patent issuing from this application.

Specification

The specification should be reviewed for improper recitation of hyperlinks. All such recitations should be deleted or amended such that the hyperlinks are rendered inactive. See MPEP § 608.01.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 131 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention appears to employ novel biological materials, specifically the cDNA deposited under ATCC accession number 209977. Since the biological materials are essential to the claimed invention they must be obtainable by a repeatable method set forth in the specification or otherwise readily available to the public. If the biological materials are not so obtainable or available, the requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the biological materials. The specification does not disclose a repeatable process to obtain the biological materials and it is not apparent if the biological materials are readily available to the public. It is noted that Applicant has deposited the biological materials, but there is no indication in the specification as to public availability. If the deposit is made under the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific biological materials have been deposited under the Budapest Treaty and that the biological materials will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit will be made (see 37 C.F.R. § 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Applicant's attention is directed to M.P.E.P. §2400 in general, and specifically to §2411.05, as well as to 37 C.F.R. § 1.809(d), wherein it is set forth that "the specification shall contain the accession number for the deposit, the date of the deposit, the name and address of the depository, and a description of the deposited material sufficient to specifically identify it and to permit examination." The specification should be amended to include this information, however, Applicant is cautioned to avoid the entry of new matter into the specification by adding any other information. Finally, Applicant is advised that the address for the ATCC has recently changed, and that the new address should appear in the specification. The new address is:

American Type Culture Collection

10801 University Boulevard

Manassas, VA 20110-2209

Claims 119-128 and 132-138 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids, vectors and host cells comprising an isolated nucleic acid comprising the full-length coding sequence of the nucleic acid sequence shown in Figure 122 (SEQ ID NO: 193), does not reasonably provide enablement for any variants thereof. Should Applicant correct the deficiencies of the biological deposit as discussed in the rejection of claim 131 above, then the specification would also be deemed enabling for the full-length coding sequence of the cDNA deposited under ATCC accession number 209951, but would not be deemed as reasonably providing enablement for any variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to isolated nucleic acids encoding the polypeptide shown in Figure 122 (SEQ ID NO: 207; "PRO1009") and fragments and variants thereof. Claims are also presented to vectors and host cells comprising these isolated nucleic acids. The specification discloses that PRO1009 is a transmembrane polypeptide (Figure 122) with sequence identity to a long chain acyl-CoA synthetase. Based on this sequence similarity, the specification asserts that PRO1009 is a new long chain acyl-CoA synthetase enzyme. A search of SEQ ID NO: 194 against publicly available sequence databases reveals that SEQ ID NO: 194 has only weak sequence similarity to prior art long chain acyl-CoA synthetases, so it is not clear that PRO1009 is truly a new member of this protein family. Also, the prior art indicates that the members of this

protein family have distinct tissue distribution and subcellular location, and are regulated independently during cellular differentiation and by diverse hormones and nuclear transcription factors. Based on these differences, each member of this protein family has distinct roles to play in lipid metabolism (see Coleman et al., 2002, J. Nutr. 132:2123-2126 for a review). The instant specification does not disclose any additional information regarding PRO1009 such as subcellular location, timing of regulation during cellular differentiation, which hormones or transcription factors regulate PRO1009, and what physiological significance PRO1009 has. Due to the large quantity of experimentation necessary to determine empirically the missing essential information about PRO1009 as a potential long chain acyl-CoA synthetase; the lack of direction/guidance presented in the specification regarding same; the absence of working examples directed to same; the complex nature of the invention; the contradictory state of the prior art (see Coleman et al.); the unpredictability of subcellular location, timing of regulation during cellular differentiation, which hormones or transcription factors regulate PRO1009, and what physiological significance PRO1009 has; and the breadth of the claims which encompass numerous fragments and variants without any activity limitations; undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope regarding its asserted use as a long chain acyl-CoA synthetase.

The specification also discloses that PRO1009 tested positive in the gene amplification assay (Example 170, pp. 539-555). This information provides an enabling disclosure for nucleic acids comprising the full length coding region of SEQ ID NO: 193

(or the full length coding region of the cDNA of the deposited sequence of ATCC accession number 209951, once Applicant resolves the imperfection of the biological deposit). Such can clearly be used as probes in cancer diagnosis, based on the data provided in the gene amplification assay. However, one skilled in the art would not expect that variants or fragments of these probes would retain specificity for the target gene sequence.

Also, degenerate variants are not enabled by this assay, since the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that antibodies that bind the recited polypeptides (encoded by the claimed degenerate variant nucleic acid sequences) would be useful for diagnosis of cancer or as a drug target. For example, Pennica et al. (1998, PNAS USA 95:14717-14722) disclose that:

> "An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." See also Konopka (1986, PNAS USA 83:4049-4052), who state that

> "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template" (see abstract).

Finally, even if gene amplification correlates with increased transcription, it does not always follow that protein levels are also amplified. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between polypeptide and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (p. 1863, second paragraph, and Figure 1). Therefore, the art indicates that it is not the norm that gene amplification, or even increased transcription, results in increased polypeptide levels. The preliminary data in the specification were not supported by analysis of mRNA or polypeptide expression.

Due to the large quantity of experimentation necessary to determine how to use fragments and variants of an isolated nucleic acid comprising the full-length coding sequence of the nucleic acid sequence shown in Figure 122 (SEQ ID NO: 193) or the full-length coding sequence of the cDNA deposited under ATCC accession number 209951, the lack of direction/guidance presented in the specification regarding such fragments and variants, the absence of working examples directed to fragments and variants, the complex nature of the invention, the state of the prior art showing that gene amplification data do not necessarily extend to variants that encode the same or similar proteins, the unpredictability of the effects of mutation on probe specificity, and the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 119-128 and 132-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to isolated nucleic acids encoding polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence, and variants and fragments thereof. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids that is defined only by sequence identity or hybridization ability.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity or hybridization ability. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 119-124, 127, 128 and 132-138 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The polypeptide identified as PRO1009 is disclosed as having multiple transmembrane domains, which would result in multiple extracellular domains (see Figure 122). Therefore, it is unclear what is meant by the recitation of "**the** extracellular domain" in the claims. Further, if the polypeptide had an extracellular domain, the recitation of "the extracellular domain"..."lacking its associated signal sequence" (claim 119, part (d), for example) is indefinite as a signal sequence is not generally considered to be part of an extracellular domain, as signal sequences are cleaved from said domains in the process of secretion from the cell.

Priority

The instant application claims priority to PCT/US00/08439; 60/141037; 09/380137; PCT/US99/12252; and 60/089000. The results of the gene amplification assay (Example 170, pp. 539-555) provides enablement for a portion of the claimed invention, as discussed above. The first disclosure of the results of this assay were in 60/141037, filed 23 June 1999. A claim's effective filing date is that date on which an enabling disclosure was provided in an application or a parent application. Therefore, the effective filing date for the instant claimed invention is deemed to be 23 June 1999.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 132-134 are rejected under 35 U.S.C. 102(b) as being anticipated by Zenno et al. (U.S. Patent 5,618,722; issued 08 April 1997).

Zenno et al. teach an isolated nucleic acid that would hybridize to a nucleic acid encoding the polypeptide of SEQ ID NO: 193 under stringent conditions (low stringency). See SEQ ID NO: 1 of Zenno et al., which has 31.6% best local similarity with SEQ ID NO: 193. The nucleic acid of Zenno et al. is at least 10 nucleotides in length. See SEQ ID NO: 1 of Zenno et al.

Claim Objections

Claims 129 and 130 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number

is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ECK

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER